

Application No.: 10/658,111  
 Response dated December 13, 2005  
 Reply to Office Action of June 15, 2005

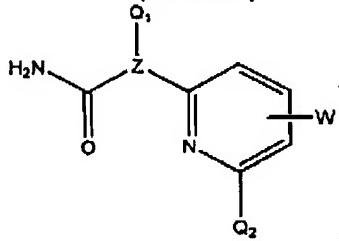
AMENDMENTS TO THE CLAIMS

Claims 11-25 and 30 are currently pending. Please amend claim 11 as indicated below. This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1-10. (Previously Canceled)

11. (Currently Amended) A compound having the formula:



, or tautomers thereof or pharmaceutically acceptable salts

thereof, wherein:

each of Q<sub>1</sub> and Q<sub>2</sub> are independently selected from 5-6 membered aromatic carbocyclic or heterocyclic ring systems, or 8-10 membered bicyclic ring systems comprising aromatic carbocyclic rings, aromatic heterocyclic rings or a combination of an aromatic carbocyclic ring and an aromatic heterocyclic ring; wherein

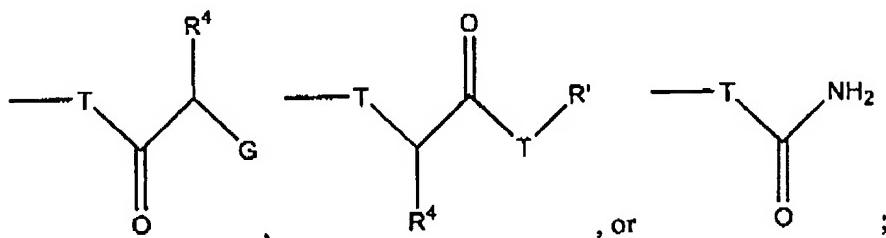
the rings that make up Q<sub>1</sub> are optionally substituted with 1 to 4 substituents, each of which is independently selected from J; halo; C<sub>1</sub>-C<sub>4</sub> alkyl optionally substituted with NR'<sub>2</sub>, OR', CO<sub>2</sub>R' or CONR'<sub>2</sub>; O-(C<sub>1</sub>-C<sub>4</sub>)-alkyl optionally substituted with A, T-C(O)R', OPO<sub>3</sub>H<sub>2</sub>, NR'<sub>2</sub>, NR'<sub>2</sub>, OR', CO<sub>2</sub>R' or CONR'<sub>2</sub>; NR'<sub>2</sub>; OCF<sub>3</sub>; CF<sub>3</sub>; NO<sub>2</sub>; CO<sub>2</sub>R'; CONR'; SR'; S(O)<sub>2</sub>N(R')<sub>2</sub>; SCF<sub>3</sub>; CN; N(R')C(O)R<sup>4</sup>; N(R')C(O)OR<sup>4</sup>; N(R')C(O)C(O)R<sup>4</sup>; N(R')S(O)<sub>2</sub>R<sup>4</sup>; N(R')R<sup>4</sup>; N(R<sup>4</sup>)<sub>2</sub>; OR<sup>4</sup>; OC(O)R<sup>4</sup>; OP(O)<sub>3</sub>H<sub>2</sub>; or N=C-N(R')<sub>2</sub>; and wherein

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the rings that make up Q<sub>2</sub> are substituted with J and optionally substituted with halo, C<sub>1</sub>-C<sub>4</sub> straight chain or branched alkyl, hydroxy, methoxy, trifluoromethyl, trifluoromethoxy, cyano, or amino;

J is a C<sub>1</sub>-C<sub>4</sub> straight chain or branched alkyl derivative substituted with 1-3 substituents selected from A, -T-C(O)R' or -OP(OH)<sub>2</sub>;

A is selected from the groups:



T is either O or NH;

G is either NH<sub>2</sub> or OH;

Z is either CH or N;

R' is selected from hydrogen, (C<sub>1</sub>-C<sub>3</sub>)-alkyl, (C<sub>2</sub>-C<sub>3</sub>)-alkenyl or alkynyl, phenyl or phenyl substituted with 1 to 3 substituents independently selected from halo, methoxy, cyano, nitro, amino, hydroxy, methyl or ethyl; or a 5-6 membered heterocyclic ring system optionally substituted with 1 to 3 substituents independently selected from halo, methoxy, cyano, nitro, amino, hydroxy, methyl or ethyl;

R<sup>3</sup> is selected from 5-6 membered aromatic carbocyclic or heterocyclic ring systems;

R<sup>4</sup> is selected from H, (C<sub>1</sub>-C<sub>4</sub>)-alkyl optionally substituted with N(R')<sub>2</sub>, OR', CO<sub>2</sub>R', CON(R')<sub>2</sub>, or SO<sub>2</sub>N(R<sup>2</sup>)<sub>2</sub>; a 5-6 membered carbocyclic or heterocyclic ring system optionally substituted with a (C<sub>1</sub>-C<sub>4</sub>) branched or straight-chain alkyl group, N(R')<sub>2</sub>, OR', CO<sub>2</sub>R', CON(R')<sub>2</sub>, or SO<sub>2</sub>N(R<sup>2</sup>)<sub>2</sub>; or a (C<sub>1</sub>-C<sub>4</sub>)-alkyl optionally substituted with the 5-6 membered carbocyclic or heterocyclic ring system optionally substituted with a (C<sub>1</sub>-C<sub>4</sub>) branched or straight-chain alkyl group, N(R')<sub>2</sub>, OR', CO<sub>2</sub>R', CON(R')<sub>2</sub>, or SO<sub>2</sub>N(R<sup>2</sup>)<sub>2</sub>;

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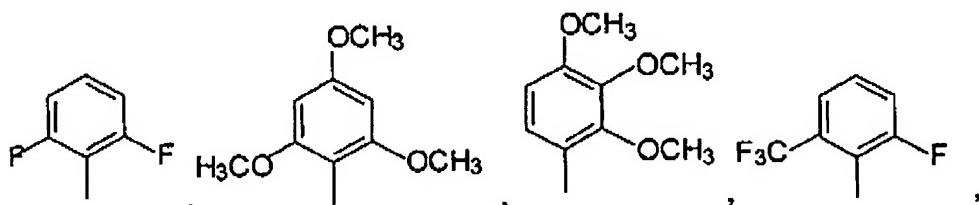
$R^2$  is selected from hydrogen, ( $C_1$ - $C_3$ )-alkyl, or ( $C_1$ - $C_3$ )-alkenyl; each optionally substituted with -N( $R'$ )<sub>2</sub>, -OR', SR', -C(O)-N( $R'$ )<sub>2</sub>, -S(O<sub>2</sub>)-N( $R'$ )<sub>2</sub>, -C(O)-OR', or  $R^3$ ; and

$W$  is selected from H; N( $R^2$ )SO<sub>2</sub>-N( $R^2$ )<sub>2</sub>; N( $R^2$ )SO<sub>2</sub>-N( $R^2$ )( $R^3$ ); N( $R^2$ )C(O)-OR<sup>2</sup>; N( $R^2$ )C(O)-N( $R^2$ )<sub>2</sub>; N( $R^2$ )C(O)-N( $R^2$ )( $R^3$ ); N( $R^2$ )C(O)-R<sup>2</sup>; N( $R^2$ )<sub>2</sub>; C(O)-R<sup>2</sup>; CH(OH)-R<sup>2</sup>; C(O)-N( $R^2$ )<sub>2</sub>; C(O)-OR<sup>2</sup>; or ( $C_1$ - $C_4$ ) straight or branched alkyl optionally substituted with A, T-(CO)R', N( $R'$ )<sub>2</sub>, OR', CO<sub>2</sub>R', CON( $R'$ )<sub>2</sub>, R<sup>3</sup>, or SO<sub>2</sub>N( $R^2$ )<sub>2</sub>; or a 5-6 membered carbocyclic or heterocyclic ring system optionally substituted with N( $R'$ )<sub>2</sub>, OR', CO<sub>2</sub>R', CON( $R'$ )<sub>2</sub>, or SO<sub>2</sub>N( $R^2$ )<sub>2</sub>.

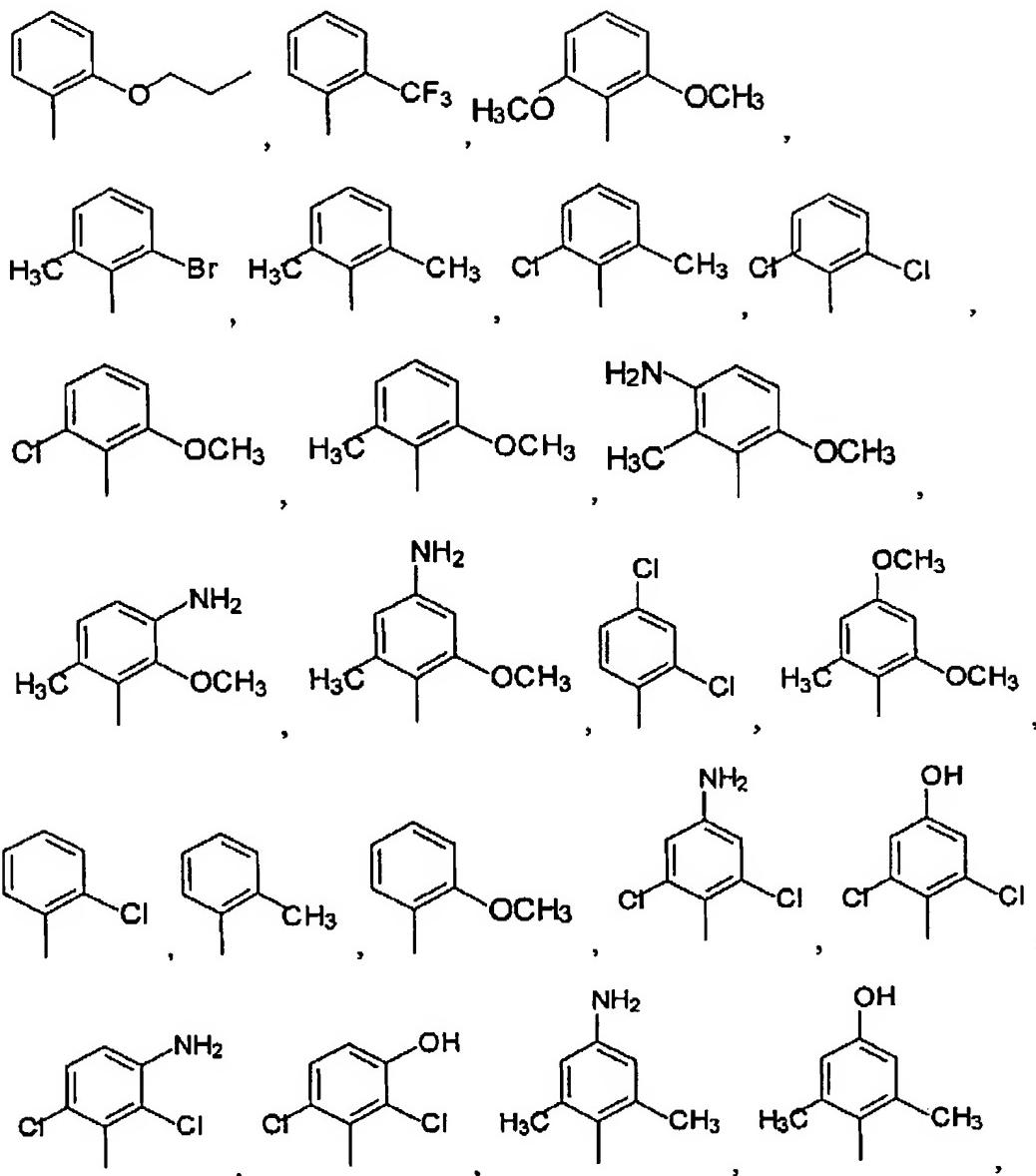
12. (Original) The compound according to claim 11, wherein Q<sub>1</sub> is selected from phenyl or pyridyl containing 1 to 3 substituents independently selected from chloro, fluoro, bromo, -CH<sub>3</sub>, -OCH<sub>3</sub>, -OH, -CF<sub>3</sub>, -OCF<sub>3</sub>, -O(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, NH<sub>2</sub>, 3,4-methylenedioxy, -N(CH<sub>3</sub>)<sub>2</sub>, -NH-S(O)<sub>2</sub>-phenyl, -NH-C(O)O-CH<sub>2</sub>-4-pyridine, -NH-C(O)CH<sub>2</sub>-morpholine, -NH-C(O)CH<sub>2</sub>-N(CH<sub>3</sub>)<sub>2</sub>, -NH-C(O)CH<sub>2</sub>-piperazine, -NH-C(O)CH<sub>2</sub>-pyrrolidine, -NH-C(O)C(O)-morpholine, -NH-C(O)C(O)-piperazine, -NH-C(O)C(O)-pyrrolidine, -O-C(O)CH<sub>2</sub>-N(CH<sub>3</sub>)<sub>2</sub>, or -O-(CH<sub>2</sub>)<sub>2</sub>-N(CH<sub>3</sub>)<sub>2</sub> and wherein at least one of said substituents is in the ortho position.

13. (Original) The compound according to claim 12, wherein Q<sub>1</sub> contains at least two substituents, both of which are in the ortho position.

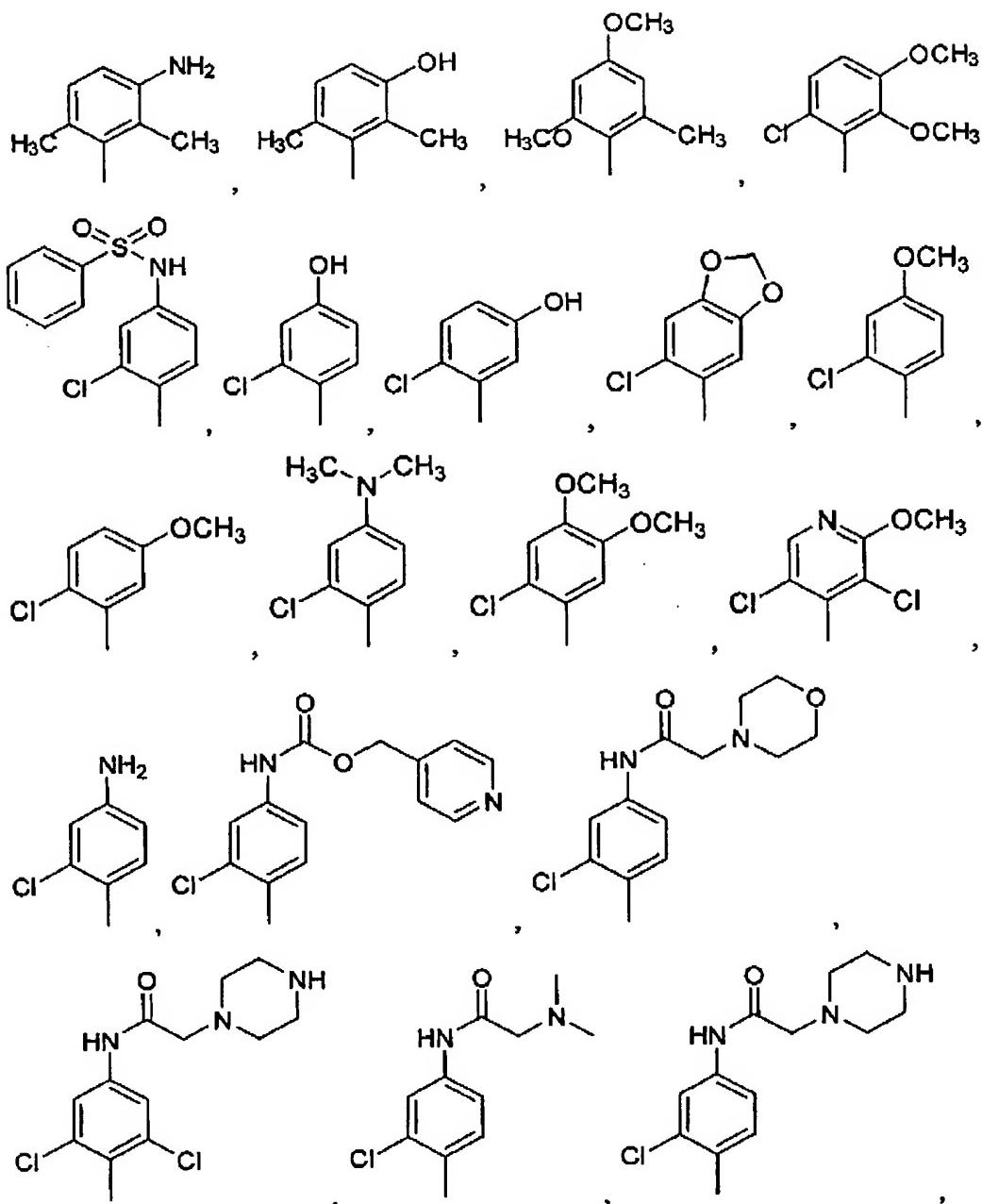
14. (Original) The compound according to claim 12, wherein Q<sub>1</sub> is selected from:



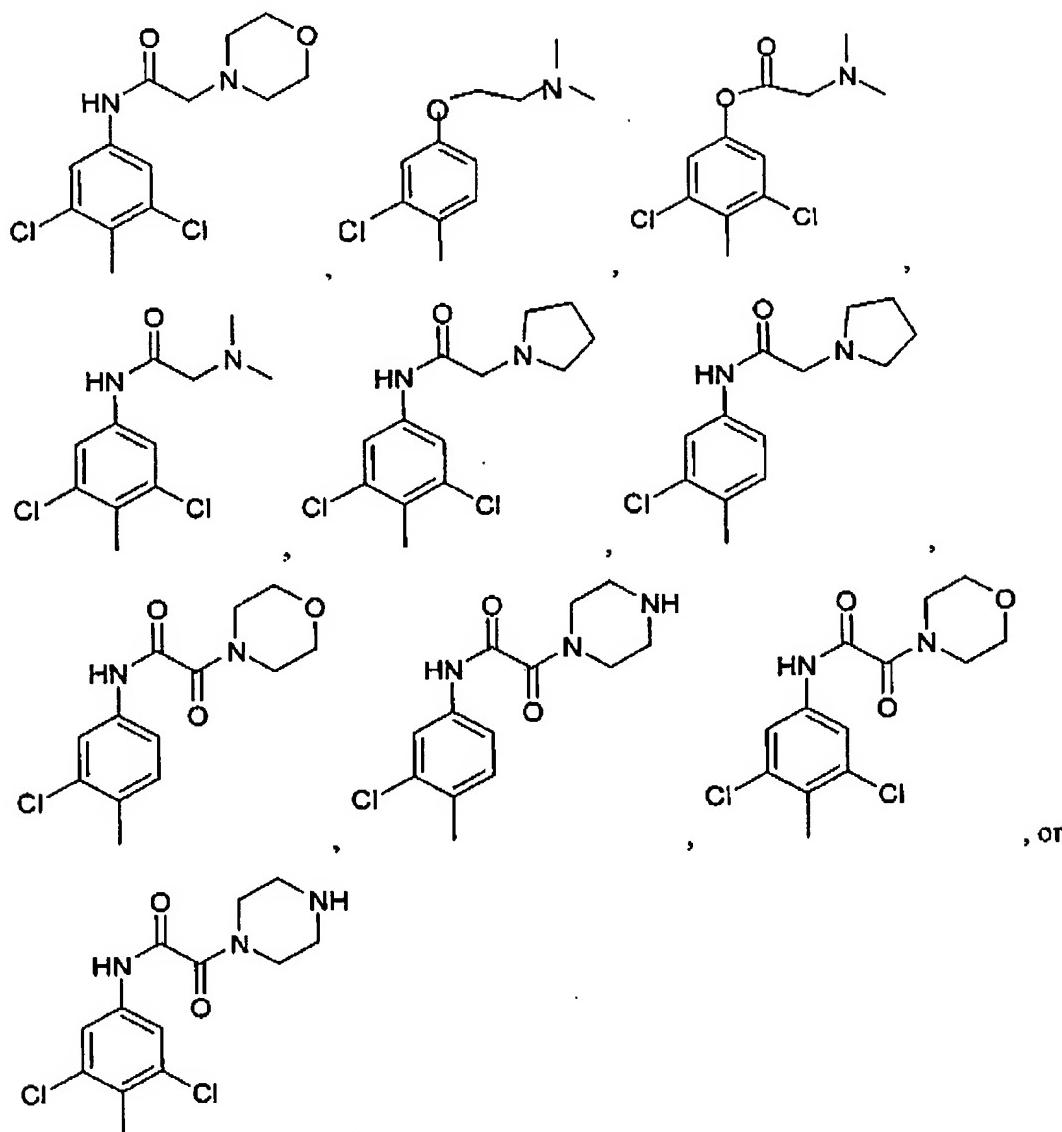
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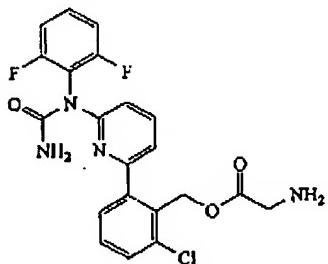
15. (Original) The compound according to claim 14, wherein Q<sub>1</sub> is selected from 2-fluoro-6-trifluoromethylphenyl; 2,6-difluorophenyl; 2,6-dichlorophenyl; 2-chloro-4-hydroxyphenyl; 2-chloro-4-aminophenyl; 2,6-dichloro-4-aminophenyl; 2,6-dichloro-3-

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aminophenyl; 2,6-dimethyl-4-hydroxyphenyl; 2-methoxy-3,5-dichloro-4-pyridyl; 2-chloro-4,5-methylenedioxy phenyl or 2-chloro-4-(N-2-morpholino-acetamido)phenyl.

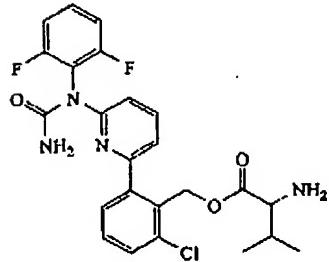
16. (Original) The compound according to claim 11 wherein Q<sub>2</sub> is selected from phenyl or pyridyl, said phenyl or said pyridyl containing the substituent J and 0 to 3 other substituents, wherein each of said other substituents is independently selected from chloro, fluoro, bromo, methyl, ethyl, isopropyl, -OCH<sub>3</sub>, -OH, -NH<sub>2</sub>, -CF<sub>3</sub>, -OCF<sub>3</sub>, -SCH<sub>3</sub>, -OCH<sub>3</sub>, -C(O)OH, -C(O)OCH<sub>3</sub>, -CH<sub>2</sub>NH<sub>2</sub>, -N(CH<sub>3</sub>)<sub>2</sub>, -CH<sub>2</sub>-pyrrolidine and -CH<sub>2</sub>OH.

17. (Original) The compound according to claim 11, wherein said compound is



### Compound 1S.

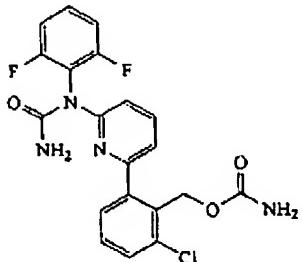
18. (Original) The compound according to claim 11, wherein said compound is



### Compound 16.

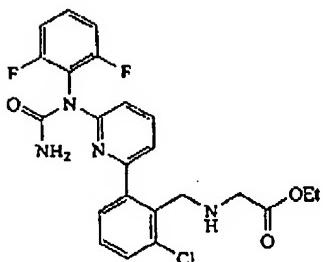
19. (Original) The compound according to claim 11, wherein said compound is

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Compound 17.

20. (Original) The compound according to claim 11, wherein said compound is



Compound 18.

21. (Previously Amended) A composition comprising a compound according to claim 11 and a pharmaceutically acceptable carrier.

22. (Previously Amended) A method of treating inflammatory diseases, destructive bone disorders, reperfusion/ischemia in stroke, myocardial ischemia, renal ischemia, cardiac hypertrophy, rheumatoid arthritis, inflammatory bowel disease, ulcerative colitis, or Crohn's disease in a patient, said method comprising administering to said patient a composition according to claim 21 in an amount effective to inhibit p38.

23. (Previously Amended) The method according to claim 22, wherein said method is used to treat an inflammatory disease selected from acute pancreatitis, chronic pancreatitis, asthma, allergies, or adult respiratory distress syndrome.

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24. (Previously Amended) The method according to claim 22, wherein said method is used to treat rheumatoid arthritis, inflammatory bowel disease, ulcerative colitis, or Crohn's disease.

25. (Previously Amended) The method according to claim 22, wherein said method is used to treat a destructive bone disorder selected from osteoarthritis, osteoporosis or multiple myeloma-related bone disorder.

26-29. (Previously Canceled)

30. (Previously Amended) The method according to claim 22, wherein said method is used to treat ischemia/reperfusion in stroke, myocardial ischemia, or renal ischemia.

31-33. (Previously Canceled)